

PART ONE
THE STABILITY OF HINDERED VINYL ALCOHOLS
PART TWO
A NEW SYNTHESIS OF CAROTENOID CHAINS

BY
PHILIP LEE SOUTHWICK
A.B., University of Nebraska, 1939
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SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN
CHEMISTRY IN THE GRADUATE SCHOOL OF
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PART ONE

THE STABILITY OF HINDERED VINYL ALCOHOLS

INTRODUCTION

The discovery of a group of stable enols^{1,2,3} in which steric hindrance rather than chelation apparently supplies the stabilizing influence has led to an effort to define the structural features which confer their exceptional resistance to ketonization. The problem has been attacked by varying the number, nature and position of the hindering groups about the vinyl alcohol structure. The present investigation is concerned with the preparation of two new stable vinyl alcohols as a part of this program. The currently available evidence indicates that stability may be expected of ketone enols bearing hindering aromatic groups in both *alpha* and *beta* positions and a third hydrocarbon substituent in the *beta* position. Enols of diarylacetaldehydes apparently require the presence of only one hindering group for stability.

Instability under oxidizing conditions has characterized many enolic compounds, and the reducing action of enols may be related to tautomerization. A second part of this investigation is concerned with the action of oxygen upon certain vinyl alcohols.

EXPERIMENTAL AND DISCUSSION OF RESULTS

The stable enol, β,β -diisodurylvinyl alcohol (I), m.p. 149.5-151.5°, was prepared by the bimolecular reduction of isoduraldehyde (II) with the magnesium-magnesium iodide reagent of Gomberg and Bachmann.⁴ Isoduraldehyde (II), m.p. 22-25°, was obtained from isodurene by use of the Adams modification⁵ of the Gattermann reaction. In addition to the vinyl alcohol I, there was isolated from the "magnesioid iodide" reduction product one of the two stereoisomeric (meso and racemic) hydroisoduroins (III), m.p. 225.5-226.5°. In other cases the bimolecular reduction of di-*ortho*-substituted benz-

aldehydes with this reagent has resulted in the formation of the corresponding hydrobenzoin,⁶ and the preparation of stable vinyl alcohols from these products has required a separate dehydration procedure.^{7,8} Dehydration of the hydroisoduroin (III) with a mixture of glacial acetic and hydrochloric acids also produced vinyl alcohol I. By treatment with benzoyl chloride and pyridine, vinyl alcohol I was converted to a benzoate, m.p. 156.5-158°. The structure of I was assigned by analogy to that of β,β -dimesitylvinyl alcohol, which Rowland⁷ prepared by a similar process and studied exhaustively.

The stable vinyl alcohol, 1-isoduryl-2-mesityl-3-phenyl-1-propen-1-ol (IV), m.p. 118.5-119.5°, was prepared by the 1-4 addition of phenylmagnesium bromide to isoduryl α -mesitylvinyl ketone.³ Vinyl alcohol IV was converted to an acetate, m.p. 133-134°, by use of acetic anhydride and pyridine, and to a benzoate (two crystalline forms; needles, m.p. 168-170°, and prisms, m.p. 184.5-185.5°) by the action of benzoyl chloride and pyridine. When oxygen was bubbled for three days through a solution of enol IV in acetone, some degradation to isodurenol and benzyl mesityl ketone occurred, but most of the material was recovered unchanged. This type of cleavage is characteristic of enols similar to 1,2-dimesityl-1-propen-1-ol⁹ but is much more rapid with the later compound than with enol IV. Oxidation of enol IV with potassium permanganate resulted in 1-4 dehydrogenation to produce isoduryl α -mesityl- β -phenylvinyl ketone (V), m.p. 148.5-149.5°. Low-pressure catalytic reduction of ketone V using Adam's catalyst apparently resulted in 1-4 hydrogenation to produce VI, the *cis-trans* isomer of enol IV. When crystallized from ethanol, VI formed solvated crystals, m.p. 51-52°, and from methanol, solvated crystals, m.p. 57°. Treatment of VI with benzoyl chloride and pyridine produced a benzoate, m.p. 179-181°, which depressed the melting points of both crystalline forms of the benzoate of IV.

The stable enol, 1,2-dimesityl-1-propen-1-ol undergoes oxidative degradation when exposed to the air for several weeks, or more rapidly when its solutions are treated with oxygen.² A study of this process⁹ has revealed that the prin-

cipal reaction leads to the formation of acetomesitylene, carbon monoxide and mesitol. Small amounts of mesitoic acid are always formed, however, indicating a simultaneous cleavage to acetomesitylene and mesitoic acid. A small amount of mesityl α -mesitylvinyl ketone is also produced by 1-4 dehydrogenation, the process which occurs when the enol is treated with oxidizing agents such as potassium permanganate.² A sixth product of the degradation, m.p. 169.5-171.5°, was not identified. It was apparently a biphenol of the formula $C_{18}H_{22}O_2$. It formed a diacetate, $C_{22}H_{26}O_4$, m.p. 148-149°, and a dibasic aryloxyacetic acid, $C_{22}H_{26}O_6$, m.p. 253.5-255.5°. The aryloxyacetic acid was found to have a neutralization equivalent of 192, as compared to the calculated value of 193.2.

The oxidative degradation of 1-duryl-2-mesityl-1-propen-1-ol followed a similar course. The chief reaction was cleavage to acetomesitylene, carbon monoxide and durenol. Duroic acid and duryl α -mesitylvinyl ketone were formed in smaller amounts. No biphenol was isolated.

BIBLIOGRAPHY

1. Fuson, Corse and McKeever, J. Am. Chem. Soc., **62**, 3250 (1940).
2. Fuson, Byers and Rabjohn, *ibid.*, **63**, 2639 (1941).
3. Fuson and Sperati, *ibid.*, **63**, 2643 (1941).
4. Gomberg and Bachmann, *ibid.*, **49**, 236 (1927).
5. Adams and Montgomery, *ibid.*, **46**, 1518 (1924).
6. Fuson, Horning, Ward, Rowland and Marsh, *ibid.*, **64**, 30 (1942).
7. Rowland, Thesis, Doctor of Philosophy, University of Illinois, 1943.
8. Ward, Thesis, Doctor of Philosophy, University of Illinois, 1942.
9. Fuson, Byers, Rachlin and Southwick, J. Am. Chem. Soc., **64**, 2336 (1942).

PART TWO

A NEW SYNTHESIS OF CAROTENOID CHAINS

INTRODUCTION

The carotenoids, that class of naturally occurring polyene pigments of which vitamin A is a member, possess extended hydrocarbon chains constructed of isoprene units. The difficulties surrounding the synthesis of such chains have been

mainly responsible for the lack of success which has attended most efforts to synthesize the natural carotenoids. The present investigation has been directed toward the development of a new method for extending a carbon chain by one isoprene unit in a single step. This result has been accomplished by the use of methyl γ -bromosenecioate in the Reformatsky reaction.

EXPERIMENTAL AND DISCUSSION OF RESULTS

Methyl γ -bromosenecioate (I) was condensed with benzaldehyde under the normal Reformatsky conditions.¹ By distillation of the product there was obtained a mixture, apparently of the expected hydroxy ester and its dehydration product, methyl β -styrylcrotonate. The yield was 53 per cent based on the methyl γ -bromosenecioate used and calculated on the assumption that the product was the hydroxy ester. Saponification of the mixture of esters with alcoholic potassium hydroxide yielded an acid, m.p. 158.5-159°, with the composition and neutralization equivalent of β -styrylcrotonic acid (II). Kohler and Heritage² reported a melting point of 153° for the acid which they obtained by means of the Reformatsky condensation of ethyl bromoacetate with benzalacetone.

Methyl γ -bromosenecioate (I), b.p. 63°/3 mm., was prepared from methallyl chloride by a series of reactions in which methallyl cyanide (III), β,γ -dibromoisovaleronitrile (IV), and methyl β,γ -dibromoisovalerate (V) were intermediates. Methallyl chloride was converted to methallyl cyanide (III) in 76 per cent yield by the use of cuprous cyanide.³ Addition of bromine to methallyl cyanide gave a nearly quantitative yield of β,γ -dibromoisovaleronitrile (IV), b.p. 89°/2-3 mm. The dibromo nitrile (IV) was converted in 54 per cent yield to methyl β,γ -dibromoisovalerate (V), b.p. 84-85°/3 mm., by heating with methanol and concentrated sulfuric acid. Dehydrobromination of the dibromo ester (V) to methyl γ -bromosenecioate (I) was accomplished in 62 per cent yield by heating and stirring a solution of V in ethyl methyl ketone with an excess of anhydrous potassium carbonate. γ -Bromosenecionitrile (VI), b.p. 84°/8 mm., was prepared in 55 per cent

yield from the dibromo nitrile (IV) by the same dehydrobromination procedure.

BIBLIOGRAPHY

1. Hauser and Breslow, "Organic Syntheses," John Wiley and Sons, Inc., New York, Vol. 21, 1941, p. 51.
2. Kohler and Heritage, Am. Chem. J., **43**, 475 (1909).
3. Tamele, Ott, Marple and Hearne, Ind. Eng. Chem., **33**, 115 (1941).

VITA

The author was born in Lincoln, Nebraska on November 15, 1916. He attended the public schools of Friend, Nebraska and was graduated from Friend High School in June, 1935. He entered the University of Nebraska the same year and was granted the Bachelor of Arts degree in June, 1939. In August of 1940 he received the Master of Arts degree from the same institution. In the fall of 1940 he entered the University of Illinois, where he held a Rohm and Haas Research Assistantship during 1940-1941, a teaching assistantship during 1941-1942, and the Abbott Fellowship during 1942-1943.

